



Cancer Research Center Hotline

Researching Nutrition and Breast Cancer

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The risk to develop breast cancer varies at least five fold around the world. Migrant women from low incidence countries to the United States experience a gradual increase in risk, suggesting that it takes more than one generation for migrants to adopt the risk of the host country and that risk factors may act early in life or *in utero*. In Hawaii¹, first generation migrant rates were already more than twice as high as rates in Japan (36 vs. 13 cases per 100,000) and increased to 57 cases per 100,000 for the second generation. While breast cancer incidence in Japan averaged approximately 28.6 per 100,000 women during 1988 to 1992², women with Japanese ancestry in the United States experienced incidence rates of 82.3 per 100,000 women as compared to 111.8 per 100,000 Caucasian women.³ Ethnic differences can be partially explained by menstrual, reproductive, and anthropometric factors, but a large proportion of the discrepancy in risk remains unexplained. A comparison between breast cancer risk factors in China and in the United States⁴ found that the combined population attributable risk was 63% for reproductive factors and anthropometric factors, leaving a large proportion of risk unexplained. Thirty years ago, it was proposed⁵ that ethnic differences were a result of environmental and life-style factors which are modified only with the passing of generations. According to this hypothesis, breast cancer risk among descendants of migrants will be similar to the risk of the host population once they have achieved full acculturation. One of the more apparent changes that migrants, in particular Asian migrants, experience over time are eating patterns. Because of the large number of Japanese migrants who came to Hawaii during the beginning of the 20th century and thanks to the Hawaii Tumor Registry established in 1960, Hawaii has been an ideal place to study the effects of nutrition on breast cancer incidence and mortality.

Early dietary research in Hawaii showed that compared to Japanese migrants¹, second generation Japanese consumed less Asian foods, such as rice, tofu, sashimi, salted fish, green tea and more Western foods, such as meat and coffee. In terms of nutrients, fat intake was higher in the second generation, while protein intake remained equal. Fat and protein intake was correlated with breast cancer in an aggregate study design⁶, but in a case-control study⁷ no strong support for the fat hypothesis was detected. A later study⁸ described an increased risk of similar magnitude among Caucasian and Japanese postmenopausal women with the consumption of sausage, meats, and dairy items, but no significant association for fat, saturated fat, or animal protein. As a result of the early dietary fat studies around the world, the WINS (Women's Intervention and Nutrition Study) was initiated.⁹ Cancer survivors, 154 women in Hawaii out of 2,400 nationwide, have been randomized to a low fat vs. regular diet to determine whether dietary fat reduction in post-menopausal women with breast cancer will decrease the relapse rate and prolong disease-free survival.

Over time, a large nutritional data base has been developed at the Cancer Research Center. It contains a food composition table with information on 132 nutrients and food components for 2200 foods, many of them based on recipes used by different ethnic groups in Hawaii. In a large multiethnic cohort of diet and cancer established in 1995¹⁰, more than 200,000 men and women in Hawaii and Los Angeles have completed a quantitative scannable food frequency questionnaire which was analyzed with the help of the nutritional data base.¹¹ This cohort study will follow more than 50,000 women of Caucasian, Japanese, and Native Hawaiian ancestry in Hawaii for many years. Data from the questionnaire will provide the opportunity to analyze the effect of different foods and nutrients on breast cancer risk. In addition, blood and urine samples will be collected and analyzed for vitamins, minerals, and phytoestrogens to determine possible associations with breast cancer risk.

In recent years, accumulated dietary research from many different populations has questioned the role of dietary fat in breast cancer etiology and lead to a shift in research focus to other aspects of nutrition. In particular, fruits and vegetables as well as soy foods¹² have been investigated as potentially protecting against the disease, whereas excess caloric intake and adult weight and gain in body mass¹³ are suspected to increase breast cancer risk through a mediating effect of insulin and related growth factors.¹⁴ Soy foods and isoflavones, phytoestrogens contained in soy products, have been a research focus at the Cancer Research Center for many years. The Analytical Laboratory at the Center has the ability to measure isoflavone levels in a variety of foods and in body fluids¹⁵ and has shown that urinary isoflavone excretion can be used as a marker of soy intake.¹⁶ A case-control study which included Asian-American women from Hawaii¹⁷ detected a 30% decreased risk of breast cancer for women born who reported eating tofu more than once a week as compared to women who ate tofu less than once a month. However, the protective effect of soy was primarily observed among women born in Asia. After completing a pilot clinical trial with isoflavone tablets, the BEAN (Breast, Estrogens, And Nutrition) study now investigates the hypothesis whether two servings of soy per day (as tofu, soy milk, soy nuts, protein isolate, or soy bar) will alter menstrual cycle length and circulating estrogen levels, which are considered predictors of breast cancer risk,¹⁸ in premenopausal women during a two-year intervention. In cooperation with several mammographic clinics, approximately 200 women have been recruited into this study so far. Comparison of mammograms at baseline and at the end of the study will provide us with information whether soy foods affect the appearance of healthy mammograms as suggested in a previous study.¹⁹ Mammographic density is an independent risk factor for breast cancer conferring an approximately fourfold risk to develop the disease²⁰ in women with a large proportion of dense areas in their mammograms when compared to women with the lowest density patterns. As part of the multiethnic cohort, a mammographic density research project will explore possible influences of soy foods and other dietary factors on mammographic densities.

An emerging area of promising research is the interaction between nutritional intake and polymorphisms in genes coding for enzymes that are involved in the chemical activation and detoxification of nutrients, carcinogens, and hormones. The interaction hypothesis may be able to explain why persons with the same genetic material

experience a low breast cancer risk in one environment and a higher breast cancer risk in a new environment. In contrast to germline mutations, such as *BRCA1* and *BRCA2*, with a low population prevalence and a strong breast cancer association, polymorphisms are present in at least one percent of the population and make people more sensitive or resistant to exogenous exposures and endogenous processes.²¹ Because of their high prevalence, they have the potential to be responsible for large numbers of breast cancers despite their relatively weak association with the disease.²² The Genetic Shared Resource at CRCH has started to explore the role of polymorphic genes that code for metabolizing enzymes in determining mammographic densities and breast cancer risk. We hope that future research in this direction will elucidate the interactive effects of genetic predisposition and nutritional patterns on breast cancer risk. For more information, please visit the Cancer Research Center of Hawaii's website at www.crch.org.

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